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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,331	01/04/2007	Shoji Takeuchi	293407US0PCT	1830
22850 7590 07/23/2010 OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, L.L.P. 1940 DUKE STREET ALEXANDRIA, VA 22314			EXAMINER ZISKA, SUZANNE E	
			ART UNIT 1619	PAPER NUMBER
			NOTIFICATION DATE 07/23/2010	DELIVERY MODE ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/586,331	Applicant(s) TAKEUCHI ET AL.	
	Examiner SUZANNE ZISKA	Art Unit 1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 January 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-19 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>7/14/06</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 7/14/06 has been considered by the examiner.

Claim Rejections - 35 USC § 103

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-19 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Vogel et al (US 2003/0146091) [Vogel].

Vogel discloses a multiaperture sample positioning system and analysis system for cells, vesicles, organelles and fragments, derivatives, mixtures thereof (Abstract) and membrane bound samples (paragraph 0041)). Vogel discloses methods for analyzing membrane proteins ([0327]). Vogel discloses the methods involve the fusion of small vesicles derived from the cell membrane (the claimed liposomes) into lipid membranes that have been formed by aut positioning giant vesicles on a carrier, followed by the subsequent electrical and/or optical analysis of the membrane proteins ([0327]). Vogel discloses the fusion of small cell derived vesicles into the bilayer ([0329]) (thus disclosing a method of forming a planar lipid-bilayer membrane for protein analysis). Vogel discloses the system may be used for direct functional analysis of membrane proteins (paragraph [0044]).

Regarding claim 1, Vogel discloses the system comprises a substrate, at least two fluid compartments and at least two electrodes. The substrate comprises a wall of electrically isolating material and may include an aperture or window (paragraph [0042]). Vogel discloses that there is an associated adhesion surface adjacent to the aperture to which samples may be bound or fixed. Vogel discloses the fluid compartments comprise a region or volume adapted to support a fluid adjacent to the aperture (paragraph [0042]). Vogel discloses the system may be used for direct functional analysis of membrane proteins (paragraph [0044]). Vogel discloses the selected assay components may include membrane-active substances, such as pore promoters, proteoliposomes and/or membrane proteins (paragraph [0045]).

Vogel discloses the fluid compartments generally comprise any region or volume adapted to support a fluid adjacent the aperture. The compartments may perform several functions, including covering the sample, providing a medium through which the cell may be moved during positioning, and/or providing a medium for establishing electrical contact between the electrodes among others. The compartments generally may have any suitable volumes, but they typically have volumes between about 0.1 to 40-100 μL . Vogel thus discloses a channel for a solution, the channel being disposed under a horizontal partition wall having an aperture (thus disclosing the claimed microchannel). See, also Figure 1 (claim 1, part a).

Vogel discloses application of the lipid solution to the aperture. Vogel discloses the system comprises a substrate, at least two fluid compartments and at least two electrodes. The substrate comprises a wall of electrically isolating material and may include an aperture or window (paragraph [0042]). Vogel discloses that there is an associated adhesion surface adjacent to the aperture to which samples may be bound or fixed. The adhesion surface is seen to be functionally analogous to the claimed liquid trap, lacking evidence to the contrary. Vogel discloses the fluid compartments comprise a region or volume adapted to support a fluid adjacent to the aperture [0042]. Vogel thus discloses the vesicle (i.e., a liposome) containing suspension is added to one or both sides of a small lipid bilayer that has been formed by autopositioning ([0331]) and the subsequent tight adhesion of a large vesicle across a small opening. Vogel discloses both sides of the bilayer are in contact with a small fluid volume that is itself in contact with electrodes ([0331]). Vogel thus discloses application of a small amount of a lipid solution to the aperture filled with a solution to form a thin layer of the lipid solution in a chamber formed at a position corresponding to the aperture of the partition wall (see, figure 1 for positioning of aperture and chamber and electrodes) (claim 1, part b).

Vogel differs from the claims in that the document fails to specifically disclose the addition of a buffer solution from the upper side. However, Vogel does disclose that fluids may be added to one or both sides of the bilayer and Vogel does disclose buffer fluids are suitable for use in the analysis (paragraph [0248]). It would have been obvious to one of ordinary skill to add buffer or other solutions as necessary to either the upper or lower side for the study and analysis of membrane proteins. The decision to add buffer or other solutions is considered to be routine optimization, dependent upon the proteins or other samples being analyzed, and a choice within the purview of one of ordinary skill in the art. See, paragraph [0260], describing the role of the fluid in the analysis. Vogel specifically discloses the use of physiological buffers. Vogel discloses the addition of fluids by pipette ([0271]), thus disclosing addition of drops, lacking evidence to the contrary. Further, the addition of the lipid as a droplet is seen to be a variation of the electropositioning method taught by Vogel as both methods result in the

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sample being positioned over the aperture, lacking evidence to the contrary (paragraph [0196]) (claim 1, part c).

Regarding claim 2, Vogel discloses controlling the thickness of the thin layer ([0269]): “The invention provides small fluid volumes that restrict the possible movement of the particles to allow positioning. For small fluid volumes of less than about 10 to 100 nl, the time required for cells or liposomes to enter the attractive range of the attractive contact zones for positioning becomes very small, and usually less than 5 minutes. The smaller the fluid volume in which the particles are suspended, the higher the chance to touch the contact zone or to enter the attractive range of this zone where charge interactions are operative. Also, the smaller the compartment size, the shorter the time required for positioning. For these reasons, the sample volumes in which the particles of interest are suspended should be as small as possible during the positioning process. Normally, the volume can be in the range from about 1 nanoliter to 500 nanoliters. Somewhat typically, the volume is from about 5 nl to 200 nl. Even more typically, the volume is from about 10 nl to 100 nl.”

Regarding claims 3 and 15, Vogel discloses the methods involve the fusion of small vesicles (the claimed liposomes) derived from the cell membrane into lipid membranes that have been formed by autopositioning giant vesicles on a carrier, followed by the subsequent electrical and/or optical analysis of the membrane proteins (paragraph [0327]). Vogel discloses the fusion of small cell derived vesicles into the bilayer (paragraph [0329]) (thus disclosing a method of forming a planar lipid-bilayer membrane for protein analysis). Vogel discloses the substance also may include detergent-solubilized proteins or proteo-liposomes of arbitrary size, with the aim of fusing them to the membrane over the aperture and thereby making arbitrary membrane proteins contained therein accessible to electrical or optical measurements (paragraph [0121]).

Regarding claims 4, 5, 12 and 13, Vogel discloses multiple apertures, thus disclosing a plurality of chambers [0083]. Vogel discloses [0086] the multiaperture system generally may include any number of measurement sites, positioned in any suitable arrangement, with any suitable size or footprint, all consistent with forming

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electric fields within each site to position and/or analyze samples. Vogel discloses the preferred configurations may be selected based on utility and/or convenience and that preferred systems may include features selected from standard microplates, so that the system may be used with standard microplate equipment, including handlers, washers, and/or readers, among others. Vogel discloses these features may include a rectangular frame, with a major dimension of about 125-130 mm, a minor dimension of about 80-90 mm, and a height of about 5-15 mm, although other dimensions are possible. The frame may include a base configured to facilitate handling and/or stacking, and/or a notch configured to facilitate receiving a cover. Vogel discloses these features also may include 96, 384, 864, 1536, 3456, or 9600 measurement sites, among others, positioned on a rectangular or hexagonal array (claims 4, 5, 12 and 13).

Regarding claims 6-8, 12, 13 and 16, Vogel discloses studying of multiple samples (paragraph [0083]) simultaneously, that the samples can be the same or different (paragraph [0084]), and that the temperature can be controlled for each sample (paragraphs [0045] and [0193]). Measurement of each sample at different temperatures is obvious in view of teachings of Vogel that each sample can be studied independently and simultaneously.

Regarding claim 9, Vogel discloses a device for forming planar lipid bilayer membranes as discussed above. Vogel discloses a substrate, a partition wall (the surface layer), a microchannel (one of the at least two fluid compartments ([0042])), a chamber with an aperture in the partition wall (figure 1), and a device for application of droplets containing the lipid solution and buffer solution. The liquid trap and adhesion surface are seen to perform the same function and therefore the claimed liquid trap is seen to be a variation in equipment design of the adhesion surface disclosed by Vogel. The microinjection device is an obvious choice for application of droplets in view of the size (nl) of the material loaded.

Regarding claim 10, Vogel discloses two electrodes, one on each side of the aperture (figure 1). Vogel does not appear to disclose "thin-film" electrodes. However, the choice of electrode is seen to a design variation and choice within the purview of one of ordinary skill in the art and dependent upon the composition to be tested.

Regarding claim 11, Vogel discloses the liquid (lipid solution) is controlled by first and second zones which control the shape and location of liquid (paragraphs [0247]-[0249]) and that the liquid should not interfere or adversely affect the analysis of the particles including electrical and optical analysis (paragraph [0260]). Vogel discloses the thickness of the lipid layer is controlled by hydrophobic forces and repulsions of each of the zones (paragraph [0254]). It would have been obvious to one of ordinary skill to control the thickness of the lipid layer in order to not interfere or adversely affect the analysis of the particles as taught by Vogel. Thus, Vogel renders obvious the claimed method of controlling the lipid layer thickness.

Regarding claim 14, Vogel discloses the addition of fluids by pipette ([0271]), thus disclosing addition of drops, lacking evidence to the contrary. Further, the addition of the lipid as a droplet over the aperture is seen to be a variation of the electro-positioning method also taught by Vogel as both methods result in the sample being positioned over the aperture, lacking evidence to the contrary (paragraph [0196]).

Regarding claim 17, Vogel discloses a device with a tapered aperture. See, for example, Figure 5. Vogel's aperture in Figure 5 resembles the aperture in Applicants' Figure 8e, for example.

Regarding claim 18, Vogel discloses the body of the apparatus is a silicon chip ([0254]) and discloses silicon etching ([0277]).

Regarding claim 19, Vogel discloses two electrodes, one on each side of the aperture (figure 1). Vogel discloses a voltage is applied between the two compartments via electrodes, and the resulting current is analyzed. Electrically tight binding means that complete coverage of the aperture is achieved. The current that results thus represents the actual membrane current mediated by transmembrane proteins and the leak currents flowing between the membrane and carrier body ([0275]).

In light of the foregoing discussion, the claimed subject matter would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill would have had a reasonable expectation of success in producing the claimed invention. Therefore, in the absence of evidence to

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the contrary, the invention as a whole is *prima facie* obvious to one of skill in the art at the time the claimed invention was made, as evidenced by the references.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUZANNE ZISKA whose telephone number is 571-272-8997. The examiner can normally be reached on Monday through Friday 9 AM to 5 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SUZANNE ZISKA/
Examiner, Art Unit 1619